Ellwein, Leon 2005

Dr. Leon Ellwein Oral History 2005

Download the PDF: Ellwein_Leon_Oral_History_2005 (PDF 96 kB)

Dr. Leon Ellwein Interview

Conducted by: Dr. Carl Kupfer
March 10, 2005

Dr. Kupfer: Today is March 10, 2005 and I am in the office of Dr. Leon Ellwein. We will be conducting an interview focusing on the international program of the National Eye Institute (NEI) from 1970 to 2000. One of the first items that I want to bring up is the fact that some programs that the Eye Institute creates a tremendous amount of conflict in the Extramural community. With respect to some clinical trials, it was very interesting to interview some outstanding laboratory researchers who felt that clinical trials was a huge waste of money that could have been better spent on fundamental research. I see this coming up all the time in terms of what had to be done with the training grant. It was looked upon as a large conspiracy to outdo departments of ophthalmology. I think that International Health could fall into the same category because I could hear individuals saying, why are you spending, even if it's only 1 to 2% of your money, on research in the developing world when we need it as much? And even today you hear the comments of why they are building schools for Iraq when we need schools here and that sort of thing. So, I thought we might start off by saying what are the advantages and disadvantages of an international program such as has been conducted by the NEI from your point of view?

Dr. Ellwein: Well Carl, my involvement in these international activities really began in the early 80s as you know when you had asked me to participate in a couple of education courses that the NEI was sponsoring in collaboration with the International Association for the Prevention of Blindness (IAPB) and my part was to pay attention to operations research and the role of operations research and health services research. So that was my first sort of engagement, and I have to—as you know those courses included clinical trials methodology, etc., etc. Some of them were done in conjunction with the American Academy of Ophthalmology a couple of times, at least in conjunction with their annual meetings. There were some clinical trials courses that were done in conjunction with ARVO and so on. So, I think first of all, all of those training activities really—and particularly those that included the international community, had a big impact and a very favorable impact, in terms of getting the international participants to really understand methodology, the importance of rigor, the importance of randomization and so on. This work was done with a minimal amount of NEI resources. These courses were two, three, four days long and so on. The next sort of move was in conjunction with our World Health Organization (WHO), the NEI's contract with the WHO

Dr. Kupfer: Do you remember roughly when that started?

Dr. Ellwein: That contract is now been going for over 25 years so it must have been initiated shortly after you became a director or the NEI was established. And I think that initially as you know, the content focused on capacity building in a very broad way because the WHO's prevention of blindness unit at that time was just being established. And this was very important I sure to them in getting it of the ground. So that contract then, about the time I came on board in 1991 we were moving it more towards a research—focused research including the first sort of major thing was a clinical trial conducted at the Arivand Eye Hospital where a comparison was made of intracapsular cataract extraction with spectacles which had been the pretty much standard treatment at the time versus the newer technology reflected in IOL implantation and extra cap extraction. And the initiative for that came out of a conference that was held about a year earlier where many people from the international eye care community were present. I remember Al Sommer was there, uh there were—we held the meeting I think in conjunction with the Pan American Ophthalmology Association—not Pan American, Asian Pacific in Katmandu. I think it was in conjunction with that meeting. And so then the NEI responded to this big question of comparing those two technologies with regard to not just outcomes, in terms of visual acuity outcomes but also patient reported outcomes, a special questionnaire was developed, a quality of life questionnaire with regard on the clinical side to complications. That study was done quickly compared to U.S. costs, maybe a 10^{th} of the cost of what something like this would have cost in the U.S. So that was I think the first major research endeavor again funded in collaboration with our WHO contract.

Dr. Kupfer: Now could we just go back in time. I'm sure you were involved in the concept of the cataract free zone in which Helen Keller Institute (HKI) was involved.

Dr. Ellwein: That is very important.

Dr. Kupfer: And that was, I think one of our very first.

Dr. Ellwein: Yeah.

Dr. Kupfer: I remember there was a meeting at Stone House and people like Newton Kara Jose said this is ridiculous, you're going to go to our university community and look for people who haven't had cataract surgery and who need it? There are no such people!

Dr. Ellwein: Yeah, that's very important and that pre-dated this randomized clinical trial of cataract surgery. This meeting that you're referring to was kind of in conjunction with Helen Keller if I remember right, because they were doing a number of things down in Latin America. And yes, there was a meeting held at the Stone House and NEI and Helen Keller joined endeavors, so to speak. A number or people from Latin America were invited to that meeting and out of it came the notion of these "cataract-free zones" where an area would be identified, an area that was considered to be under-served. Where there would be probably, quite a high prevalence of blindness because of cataract. And the question was whether one could target those areas with an intensive campaign, publicity, motivation, and free surgery. And the two—the first projects, there were two of them, one was in Brazil and one was in Peru. And again the results of that work was published and it showed that indeed there was, as you mentioned, there was indeed a cataract blindness problem in these areas even though the ophthalmologists and the eye care community didn't appreciate that. Partly because they only saw what comes to their office in terms of eye care needs. And the under-served by definition they didn't see. So that was a turning point which I then might these things were supported. The field work was supported by Helen Keller, but they were supporting it because the National Eye Institute was involved in the sort of technical side of things and the data collection and the data analysis and the generation of the publications. And an important part of that work was then the follow on when the Lions Clubs of the international foundation initiated this Sight First program which was over a hundred-million dollar program which was just coming into his final stages now, but it started in the early 90s I guess—mid 90s. And for Latin America, the Sight First program has continued to concentrate on cataract eradication along the lines of these early cataract-free zones. So, there's a case where the NEI's involvement from a technical side was really leveraged into a lot of activity by non-government organizations. And again, I think it's fair to say without the NEI's involvement this whole cataract-free zone, this whole cataract program in Latin America would not have taken off at least not in the way that it did.

Dr. Kupfer: I agree with what you say, but it's interesting when one talks to Harry Quigley, he was at the kick-off of the Cogan Collection and he made some side remarks about what role the NEI had in the international health scene and I didn't pursue it because he was minimizing NEI's role. But I'm sure there are other people like that. I'm sure Foster thinks that we were peripheral and certainly the Christoffel Blindenmssion, [Christian Blind Mission] I think has the idea that they represent the leadership role.

Dr. Ellwein: I think Carl that that's another important part and I would say that that's intentional. We—our approach, your approach, my approach was not to come in and try to dominate the situation but to some extent being in the background quietly working with the principles getting their name out front. They're in the field, they're doing the work and for example putting their name first on the publications. Yeah, we could have come in and tried to make a big splash, but that wouldn't have created the confidence, and the cooperation and the collaborative spirit that really took place and it's because we were truly in a partnership where in deed as far as the outsiders, some of them may not even know that we were present. And I think that's an important ingredient in why these things were that successful that we weren't trying to overshadow them in any way.

Dr. Kupfer: Good point. Another point that I'd very much appreciate your thoughts on is the relationship with WHO. The outside community probably wanted to know why we were contracting with WHO, giving them the money and then we go ahead and spend money to do the work. They don't realize that the money we give to WHO was what pays for the work we do. And I don't know how delicately we should approach this topic. I'm not sure there is any other institute that has a contract with WHO at NIH.

Dr. Ellwein: Well, I think—I don't know about the contract situation with other institutes. Maybe from time to time they've had some small contracts. Certainly, there are other institutes that are WHO collaborating centers. Like the NEI was a collaborating center in the prevention of blindness area. In terms of this long-standing contract, yes, I would say that at least initially it wasn't apparent that the WHO work that they were doing under the contract was possible only because of our funding because it wasn't really maybe made obvious. But in more recent years where were generating publications because the work was more research oriented, each publication of course acknowledges the NEI's financial support. So, in terms of—as all publications that are supported by the NIH acknowledge the funding source. It's pretty explicit where the support has come from and in large measure the WHO's activities in epidemiological research over the past 10 years or so have been funded by the NEI. I'd like to say that other participants haven't been involved. Some of the NGOs have joined in on a couple of the projects which is important.

Dr. Kupfer: But we were actually supporting the salary for some at the WHO with whom we interacted and I think the NGO went that far.

Dr. Ellwein: Yes, I think that's clear—and that's the part that's probably not apparent that they were and today yet where we're supporting its down to like 10% or 15% or 20% of a professional person and about a 1/3 or 40% of a secretarial support or administrative person. But yeah, in the beginning there was a full-time professional that was supported us and a full time assistant, administrative, clerical person.

Dr. Kupfer: Well I think it's easy to avoid the people who are going to be looking for things to complain about.

Dr. Ellwein: But even in terms of today, you know the NEI has been through a conference grant with ARVO. Has supported a US/NDO conference to look at research collaborations that not necessarily epidemiological, but pre-clinical, clinical studies and this is only possible because the international community does know about the NEI, is aware that the NEI is and has been a player, a contributor to the international scene including a lot of activity in India and as a result there's probably going to be a new NDO/US agreement between the government of the U.S. and the government of India. On the U.S. side it will be signed by Dr. Zerhouni and on the India side, his counterpart, the head of the Department of Biotechnology. And again this will be of great benefit to the Extramural community in terms of making collaborations with Indian investigators easier. Easier in terms of Indian government approval of collaborative projects. Indian government approval of material, samples, clinical materials, going back and forth. And it's been possible because of our—the NEI's long-standing relationship and activities in India.

Dr. Kupfer: Was Dr. Zerhouni at that meeting?

Dr. Ellwein: Dr. Zerhouni was not at the meeting but the plan is to have this agreement signed at ARVO on May 1st when Dr. Zerhouni will be at ARVO as a plenary speaker. And the Indian counterparts will be there as well.

Dr. Kupfer: Really?

Dr. Ellwein: Yes, they're coming over for that event.

Dr. Kupfer: Great. That's great. You will be primarily involved with that?

Dr. Ellwein: Yeah, I will, well, the intent here is to create a document, a Letter of Intent, whatever it's called so that our grantee communities, in their research interests, and their research collaborations are facilitated. There is no intent at this point to set aside a specific amount of funds for this collaboration but the fact is that by connecting up researchers on the Indian side and the U.S.side that they will be very competitive in generating a regular RO1 type of grants. And as you know the advantages on the Indian side are an abundance of clinical material and a very favorable cost structure, of very low costs. On the U.S. side, we're maybe a little bit ahead on some of the technologies maybe we're ahead on the ability to write and develop and to document or create the research proposals that get through the peer review system. So I think that it's promising and again I think that it is one of the pieces in this long 30-year history of paying attention to the international setting.

Dr. Kupfer: What about specimens? Will this agreement allow specimens to be sent to the United States?

Dr. Ellwein: Yeah. It doesn't speak about it specifically it just talks about a transfer of materials where appropriate. So each case would be handled on its own.

Dr. Kupfer: Right.

Dr. Ellwein: But nevertheless, having such an agreement in place will certainly facilitate this kind of thing. The idea is not for US researchers simply to do Fed Ex research. Suck up materials and bring them over here, but again, really on a very collaborative mode where much of the research activity, the analysis, the laboratory work would be done over there.

Dr. Kupfer: And all of these grants will go through peer review and be cleared by the Council?

Dr. Ellwein: Yeah exactly.

Dr. Kupfer: Right. One of the things about the NEI program as compared to NGOs is that we really focused on two or three countries, whereas you take HKI, I think they're active in a large number of countries as is CBN. And we were particularly interested in doing a project which then could serve as a model for others to think about in pursuing their own research.

Dr. Ellwein: Yes, I think there is kind of a little bit of background that explains this focus. Again it pertains specifically I would say to our collaborations and doing work through WHO. Is that as we move toward research activities we moved into—there was as you know in Nepal a large blindness prevalence survey done in the early 80s. Save-A-Foundation, one of the NGOs came to us and asked to do a follow up. And we said why do a follow-up, but we looked at certain areas in Nepal, a part of the country and we included some ingredients that were not in the original one and particularly the outcomes on those that already had cataract surgery. Namely clinical outcomes as well as quality of life outcomes.

Dr. Kupfer: And that was Lumbini?

Dr. Ellwein: Lumbini was one of the districts. Now what…and we worked with Dr. Pokerol (sp?) who was one of the principle investigators at the Katmandu Eye Hospital and who is now at WHO. That adult survey was replicated with the same kind of protocol in China. When we went to China we asked ourselves who in China could do a good job. Who was capable of really conducting research in a fashion that we would find acceptable and we turned to Dr. Jah Ling Jouh (sp) who had spent a year or so here at around 1991 and he then carried out this survey near Beijing and did an excellent job. Dr. Jouh today is the President today of the Chinese Ophthalmology Society and we continue to work with him. We also conducted using the same protocol, the surveys in adults down in India and there again we went to people that we had dealt with before—investigators, clinical field workers at the Arivand Hospital at the L.V. Prasad and at the R.P. Center in Delhi. Our emphasis was, what team could carry out the research and the purpose was to carry out this research that matches international standards of quality. Western standards of quality in terms of rigor. And that's the way these things were done and it's evidenced by the findings in all of these surveys being published in the usual peer-reviewed journals. American Journal of Ophthalmology, Ophthalmology, ARVO's journal and so on. And then as you know, in collaboration with WHO, we shifted from surveys in adults to surveys in children. And again that was possible because of our strong relationship with the WHO. I remember you and I in about 1997 or something and talking about he neglected area in terms of not knowing much about the magnitude of the vision impairment problem in children. And as a result we moved into that area by first documenting the appropriate protocol in detail and then carrying it out. First in three places, places were again we had competent investigators. We went back to China, we went back to Nepal and we included Chili and South America. Those three studies, the results were sufficiently interesting and surprising in the sense of that not just the magnitude of refractive error in children which varied greatly but the fact that roughly half of the children who needed refractive correction did not have it and tha those findings were of great interest to the international community and provided sort of the rational for expanding. People would say what about India, what about South Africa, what about Malaysia, what about Southern China? To date eight such studies have been completed. And the publication for the last one which was in Malaysiais going to appear in a month or so.

Dr. Kupfer: Now this is very interesting to me because what I think I'm hearing is that the role of the NEI was to bring its technical expertise to bear on doing a model program and then allowing the NGOs to decide whether they wanted to pursue this further.

Dr. Ellwein: Yes.

Dr. Kupfer: The NEI isn't involved in the Malaysia one or the South Africa one?

Dr. Ellwein: The NEI, through the WHO did fund the Malaysia one.

Dr. Kupfer: Oh.

Dr. Ellwein: The South Africa one—in all of these we funded a technical oversight committee which I was the chairman of. It's the same committee—it really started with the three original PIs from the three original projects. We stayed together and then provide oversight and sort of analysis capability to the others. The Malaysia was funded by us through WHO.

Dr. Kupfer: It was more than just the technical oversight.

Dr. Ellwein: Yes, more than just the technical oversight. These projects cost about $100,000 each. Again, a project, $100,000 each doing something comparable in a Western country would be twenty times that.

Dr. Kupfer: But there were no NGOs that wanted to pick it up?

Dr. Ellwein: In South Africa the project there was supported by the ECCE and in Australia, the International Center for Eye Care and Brian Holden is the head of it, yes.

Dr. Kupfer: I see. I see.

Dr. Ellwein: It was, they provided most of the research funding for the field work, but in addition to that CBM kicked in and SightSavers kicked in. So there was a case where all three came into it. These kinds of projects.

Dr. Kupfer: You ran the review committee?

Dr. Ellwein: We ran the Oversight Committee.

Dr. Kupfer: So that was acceptable?

Dr. Ellwein: Yes, and quite frankly handled all of the data, management analysis, cleaning at to-to really writing the papers.

Dr. Kupfer: Who did that in the association with you?

Dr. Ellwein: Well, in each case I was sort of the chief scribe and they, the people in the field were, they essentially did the field work.

Dr. Kupfer: But you handled all the data analysis?

Dr. Ellwein: Since these eight places were—you can call it eight studies or you can say one study conducted at eight sites. And when you look at it as one study conducted at eight sites we used exactly the same data analysis software at each place, which was developed originally for the original three. It was just a matter of rerunning the programs. It was not quite that simple, but rerunning the programs and analyzing each site using the same software.

Dr. Kupfer: I guess what I'm getting at again, is to focus on the NEI's contribution. And I know you've been involved very heavily but is there anyone else at NEI that may have worked on this or…I remember there was a biostatistician from Chili.

Dr. Ellwein: Yeah, with Chili, one of the people who was involved in the Chili project was Dr. William Yost and he stayed on the advisory committee and was quite involved in the analysis—in developing the software programs and in the analysis.

Dr. Kupfer: And was he paid by the NEI?

Dr. Ellwein: And his role, he had—for the initial three he was called the Data Center and so with a small contract through the WHO relating to the first three projects he was the Data Analysis and Management Center. And then after that once all these programs were developed, he stayed on board as a part of the Advisory and Oversight Committee. But these projects were really research projects and it's not quite the kind of thing that the usual NGOs are interested in. They're interested in service, service that might have a little bit of a research component, a little bit of an evaluation component but this is not their main area of interest and focus. So they, on the one hand—and secondly, they probably wouldn't be able to bring the scientific rigor to a project even if they were interested in expanding in this kind of area.

Dr. Kupfer: Well, I guess what I'm getting at, I haven't made it clear is that my view is that the NGOs for instance have been and still may be resistant to evaluation of what they do. And the NGO really laid out pretty clearly how to go about evaluating (laughter), and the question is, has that taken hold?

Dr. Ellwein: Well, I think they are somewhat resistant to evaluation. Not just because it uses funds that maybe could be used for service but sometimes the evaluation points out and raises questions that are uncomfortable to deal with. For example, when we did the cataract—the adult surveys focusing on cataract in India and China and Nepal, you know the outcomes that we were seeing in these population-based surveys was certainly not what was expected. The outcomes were far below what many people thought. The idea was, you operate on a cataract and that equated to sight restoration. And these surveys that were done very carefully in an unbiased fashion in representative populations demonstrated that it wasn't quite that clean of a relationship between an operated eye as a sight as an eye that has sight restored.

Dr. Kupfer: Right.

Dr. Ellwein: And so that kind of message doesn't really go very far in an NGO's fund raising activities for example. But! In terms of them reformulating a program, paying a lot of attention to outcomes, being careful on whom you operate on, it then does have a potential high-value for the service delivery component. And indeed I think, for these adult cataract programs, outcomes, is now a common element in any service program. Maybe not so much in formal evaluation, certainly in children, this notion that a lot of school-aged children are without the necessary spectacles or are with spectacles that are not appropriate has really caught on the in the community and it gives them something to kind of grab a hold of. It gives them sort of a scientific underpinning for initiatives that for the NGO as they move into the areas. And I think they too, they see the research as not being their area of interest or responsibility. Unfortunately there really are not organizations that are funding international—research on an international scale, at least not in the vision area, other than you know, what the NEI's doing and what a few organizations maybe in Europe are up to.

Dr. Kupfer: Just to go back a moment because as you pointed out your first area of concentration was in operations research and again it seems to me that the problems of how do you identify the patients. How do you bring them to the central hospital to operate? Early information that if you had a hundred patients who were blind from cataracts in the community and you told them to come to Arivand and well, 50% would show up and that has now improved considerably though your efforts and the efforts of Arivand. But I'm sure that that lesson has spread to the NGOs.

Dr. Ellwein: Yes it has…

Dr. Kupfer: Well, maybe it hasn't because then there's the story about the CBM hospital in Nepal, that's right on the border with India. I forget who ran it-- an ophthalmologist.

Dr. Ellwein: Yeah, right.

Dr. Kupfer: And I remember whispering to me that the ophthalmologist would have everyone come at 6 AM in the morning and they would stand for three hours in the hot sun before they would start being screened. So that the ones who really wanted to have the surgery would remain and the others left. That's not exactly a Leon Ellwein model (laughter).

Dr. Ellwein: You know I think on that issue Carl, another important finding from these research projects. I remember this whole notion of coverage and that—I remember when we were being encouraged to do an assessment in Nepal, the idea was when we would go back into Nepal we would find that blindness because of cataract had been eliminated. That coverage was sort-of-speak, 100%. And indeed when we went back, not doing the whole country but sampled these two districts as we mentioned earlier, the coverage was good but nothing along—approaching 100% by any means. I think, the thinking now is that if two-thirds of those that were effected received cataract surgery that's a high number. And people for a variety of reasons don't come for cataract surgery. They maybe have spoken to someone who had a bad outcome, in this business of outcomes as a big driver. They may unfortunately be in a situation where they can't afford it or have no one to accompany them although in some institutions like the Arivand and others in other institutions in India there's free cataract surgery for those who cannot afford it. This is not the case for example in China and in most other places. They may just feel that they were destined to be blind, and this is God's will and they shouldn't tamper with it, and so on and so on, and so on.

Dr. Kupfer: Right.

Dr. Ellwein: And so the notion that one can even within any kind of an intensive program is reached the point where a 100% of people are free from cataract blindness is not realistic. There will always be a so-called "backlog." Now the idea is to minimize the backlog and as I mentioned, delivering good outcomes is one of the ways to increase the confidence in the community. You know you didn't mention the World Bank Project in India.

Dr. Kupfer: I was getting to that.

Dr. Ellwein: And the World Bank Project in India came about again for—because of what had been done in some of these surveys in India with regard to blindness because of cataract. It came about because the government of India's interest in this problem which in India, the cataract blindness project seems to start at an earlier age. And as you know WHO was involved and the NEI was involved. That is to say that the World Bank then came to the NEI for technical advice and guidance from the beginning they came to us in what they called the program development phase and then we stayed with them throughout the project and through the periodic evaluations and so there again the NEI with a small amount of resources, mainly in this case the time of you and my time and Ed McManus was involved in a couple of the trips, we had a pretty major influence on what turned out to be a hundred million program for cataract eradication—cataract services in India.

Dr. Kupfer: Now may I just interrupt for a moment?

Dr. Ellwein: Yeah.

Dr. Kupfer: The basis for knowing that the cataract blindness was an important consideration was the results of Indian assessments. There were at least two of them I believe.

Dr. Ellwein: Right, there were some earlier Indian prevalence surveys that provided very useful information. The documentation and the rigor in which these early assessments were carried out were not quite as extensive and rigorous as what we did when we carried out those surveys in the early 90s, the ones that were in collaboration with the WHO. But since those were government surveys, those early ones, it provided kind of the government, the basis for the government's interests. And then our surveys that came along later in very specific areas, certain districts of India, again emphasized the importance of outcomes, which hadn't been addressed at all in the early government surveys. As well as ensuring that in a survey you get a high response to the examinations, by first going door to door identifying everybody over the—of the appropriate age. In this case were looking at people age 50 and above. And then making sure that they participate in the research by coming and having the eye examinations so that you don't end up with a biased group that those that have a problem either are not showing up or those that don't have a problem not showing up and therefore your results are very hard to interpret and generalize. And again I want to emphasize that because the early studies it was never really clear to what extent the people that were examined were truly representative and had a minimum of self selection bias.

Dr. Kupfer: Has there been anything published about the World Bank study?

Dr. Ellwein: The World Bank, uh, has never—the World Bank's efforts, which were service oriented. It was the government of India, as you know, set up a office, it already had been there but expanded it and they set up what they called these blindness control societies in each district starting first with the nine what was it? Nine—seven states or nine states that the World Bank project included, but then the government wanted to expand it into the whole of India. So they would be collecting statistics on how many had been operated on, the equipment had been purchased, the infrastructure upgrades etc. etc. But again the data were simply, mainly on operated cases and there was really, as part of the formal program, there was really not a concerted effort to really dig into outcomes. Because this would have required, what you call in terms of people coming back and so on. But as we did with support from the World Bank, we conducted a project in Rajasthan where the field work was supported by the World Bank and we provided again, the technical oversight. One in in Rajasthan and one down in the south in the Sevagunda (?) District. So, those two districts were population-based surveys were done and the idea was to look at the potential impact of this new emphasis on cataract surgery. And the bottom line was the Rajasthan area was in trouble and the Sevagunda (?) area, things were pretty good.

Dr. Kupfer: Do you have a list of all the reprints?

Dr. Ellwein: Yes.

Dr. Kupfer: \I think that that should be an appendix in the book.

Dr. Ellwein: Yes. Indeed, the WHO had what they call a consultation about a year and a half ago where they brought the WHO collaborating centers together and the idea was coming together and thinking about—reviewing what had been done and what priorities for the future would be. And as part of that meeting I presented, I had prepared a set of slides that included tables of where all these studies over the past 10 years had been done and the publications that resulted. So that information is easy to provide. It could be an appendix.

Dr. Kupfer: Okay.

Dr. Ellwein: The light's blinking here, is it?

Dr. Kupfer: That's when we talk. I think that about 1999 NIH had a meeting in which each institute would present their international programs and it was really interested because we were the only ones that published the stuff that we did. Occasionally Infectious Disease would do it, Mental Health never did it. Cancer would occasionally do it and I remember Phil Shambra came up to me and he said, "Boy, I wish all institutes would do it the way the NEI did it and published this stuff." Well, I guess the question that will really dominate the entire chapter will relate to how important the limited focus research is.

Dr. Kupfer: We will continue.

Dr. Ellwein: Yeah Carl, looking—sort of looking to the future, it seems like, and the past has been concentrated even before I came there was a case-controlled study in China that Bob Sperduto and Dr. Jowar (sp) were involved in.

Dr. Kupfer: A case controlled study?

Dr. Ellwein: Yes.

Dr. Kupfer: I don't remember that, I remember a clinical trial in which patients were randomized.

Dr. Ellwein: No, they did some sort of risk-factor thing, I think. You know there were some collaborations with the Nutrition Institute in India and so on…

Dr. Kupfer: Oh yes, yes.

Dr. Ellwein: Yes, and these things I'm not familiar with because I wasn't here at that time. But in thinking about this, you know we've done studies that have been of an epidemiological nature in terms of the problem, characterizing the problem, understanding the problem… but it seems like and we've looked at as we've mentioned, adults, children. But I think in the future the emphasis needs to be on more traditional clinical research, traditional, basic science collaborations. And shift it away from epidemiology and understanding the problem to try to do something about it in terms of new interventions, new management strategies and so on. And this is where as I mentioned this NDO/US agreement, you know—the emphasis is on preclinical basic science, genetics, and so on. And I think that those are the collaborations that are where the actions should be for the future. And there's just the studying the problem, the magnitude of the problem is helpful, particularly in the country, you know, for the country to do something about it. But as we get into this other kind of research through traditional biomedical research, the findings there are just automatically relevant to the world as a whole.

Dr. Kupfer: That's right.

Dr. Ellwein: And you know finding something about poor outcomes in India for cataract surgery, well, do we have better outcomes here in the US or not? Well, I don't know, maybe not.

Dr. Kupfer: We had the Neon Program.

Dr. Ellwein: Yeah, the Neon Program stopped because people didn't to report their outcomes. The cataract surgery outcomes that were found in the LALES study, the Los Angeles Latino Eye Survey out in the Los Angeles area conducted by USC. The cataract surgery outcomes are essentially not that different from the better parts of India. Which is still not "one-eye-operated, is-one-eye-sight-restored" level by any means. But anyway so just to say it again, I think that's where we need to move toward. And that means, you know, trying to engage our entire extramural community in this area. And as you know, ARVO's membership is 40% international. Not necessarily developing countries, they're probably underrepresented in the ARVO membership but there is a potential there for international collaborations. And if you mentioned the NEI spending 2-3% of their budget, well, it's hardly that. Our six hundred-million-dollar budget or seven hundred million. One percent of that would be six or seven million. We're coming no where close to spending a percent on the international thing—not even close. Now if you define things loosely maybe you can get up to a ½ of a percent, but I'm not sure.

Dr. Kupfer: What about the studies being conducted or perhaps even completed at Aravind by the group in San Francisco. They're actually doing clinical trials on cataract. I forget what the variables are…

Dr. Ellwein: You mean the Proctor Foundation?

Dr. Kupfer: Yes.

Dr. Ellwein: Places like the Aravind, like the L.V. Prasad, two private eye hospitals that the NEI has had a long relationship with. They conduct studies in collaboration with other organizations like the Proctor Foundation. I don't know the details. They're involved in some industry-sponsored studies, looking at the toxicity of different drugs, uh, for some companies to market their products in India they have to have sort of independent studies and their involved in those. At the L.V. Prasad, Dr. Roul's place, you know they've had a lot of work with the contact lens industry in looking at complications relating to toxicities related to contact lenses. And certainly our early efforts with these places in terms of research and research rigor have given them a reputation that allows them to move into other areas.

Dr. Kupfer: However, you mentioned that the future should be clinical trials and here we have the Proctor doing the clinical trials….

Dr. Ellwein: Yeah.

Dr. Kupfer: No one seems to know what's involved, uh I wanted to when Dr. V was here, Dr. Venkataswamy (sp) he didn't know anything more about that than I. So, I know it's being done on a shoe string because Proctor has approached me back in '98 or '99 just before I stepped down and said was there any way that they could get money for this. This is a concern of mine because will this be the sort of thing that will dilute the impact of what you' ve established there in terms of very careful scientific evaluation of a bad situation?

Dr. Ellwein: Well, I don't know anything about the details of it. I think just the fact that there is some activity is potentially good. If it was really shabby than it wouldn't be so good. But I think what's, what's in danger—what's, if you don't have somebody sort of championing these international activities, these international research projects, they're not going to happen. Uh, when you were the Director, you had a great interest in these kinds of things. Seeing the potential, seeing the importance of it which sometimes is a little hard to explain and describe to the skeptic because the benefits may not be immediate. And it takes somebody that really is driving these kinds of things and you mentioned the other institutes maybe not having the same level of activity or publications. And maybe its for a number of reasons, the Director hasn't been quite given at the same priority as the other institutes, the staff people maybe quite having had the contacts and the relationships to carry out this research. It takes…I certainly could not have come here in '91 and jumped into this had there not been a 15-year history preceding my coming here. It's sort of let—people knew who the NEI was. Knew who you were. Knew about your tenure as the President of the International Agency for the Prevention of Blindness and all of those activities, uh, not to mention the Pan American Association of Ophthalmology and so on and so forth. And all those associations, all of those connections, all of those engagements that showed a strong interest in the international community are really pivotal to doing anything. And that's what it comes down to. Getting back to something we said earlier—and not doing it sometimes behind the scenes in a very collaborative way, equal partnerships, not being grabbing of the headlines, not being grabbing of the first authors on the publications. Where they really see—where they think they came out ahead of the—on top, and from our perspective, we also came out on top. Everybody coming into these things if they're done right, feels that they've benefited through the greatest amount.

Dr. Kupfer: What's the future of the Lions' Program?

Dr. Ellwein: Well, the Lions—yeah, there's another, another good example. When the Lions of course established their SightFirst program back in the early '90s, '93 or '94, whenever it was. They came to the NEI, to you and to seek sort of technical direction, technical perspective, along with the WHO because the international perspective was important for the Lions. The initial SightFirst phase is about over. Uh, 150 million or whatever the expenditure has been. And now they're contemplating a SightFirst II, which will be possible by a campaign that they're planning to raise $200 million and then that will be followed by implementing projects, again throughout the world. Maybe with a little different emphasis. The emphasis on the first part was heavily emphasized in cataract inIndia,Latin America and other places. The new emphasis will probably pay a lot of attention to refractive error in children because of our projects that have demonstrated a need for refractive correction in school-aged children. So the Lions may end up putting, $50, $60, $70, $100 million dollars into this area. The importance of which is now appreciated world wide. And the Lions continue to involve the NEI and the WHO. I'm a technical advisor for the Americas and the WHO is, I mean the secretary, and the technical advisor that reviews the proposals for funding and so on.

Dr. Kupfer: On the SightFirst committee there really isn't a very strong research credentials now…

Dr. Ellwein: Well, I don't know that that's such a deficit. Again, the Lions are service oriented. When they spend their money, they're doing service projects. Now they want to conduct projects that make sense. That have again, some sort of scientific underpinning that assures them that the service will do some good. But as far as revealing the projects themselves, is mainly, is the need there, uh can the Lions do the work? What about their eye care provider collaborators, the ophthalmologists that are involved in the project, what's their commitment? When its alls aid and done the Lions of course are interested in conducting projects, in having a community awareness, having a community perspective that helps them attract new members and so on. But again, when they move into an area like refractive error in children or diabetic retinopathy, they move into these areas knowing that the NEI supports research findings, that these are areas that make sense and that something can be done about it.

Dr. Kupfer: What's going to happen to the cataract program in Latin America?

Dr. Ellwein: I think the cataract program in Latin America will be shifting. The SightFirst program in Latin America will be shifting from cataract to diabetic retinopathy to refractive error in children and the cataract campaigns themselves will probably not be to the highest priority. Partly because each country has had, I don't know—5, 6, 7, 8, 9, 10 projects? The community is quite aware of the Lions and their efforts and cataract is something that will always be around, and projects forever, but they—you can say well maybe these are more like demonstrations, so now they want to move into diabetic retinopathy and demonstrate where the community can get involved. And the same thing with refractive error in children.

Dr. Kupfer: Diabetic retinopathy looks simple but…

Dr. Ellwein: That's right. I think they'd better stick with refractive error in children which isn't simple either but maybe a little simpler.

Dr. Kupfer: No—it's doable.

Dr. Ellwein: It's doable, yeah.

Dr. Kupfer: Well, that's a great review.

Dr. Ellwein: Yeah.

Dr. Kupfer: I think that's very, very helpful…

Dr. Ellwein: I think Carl again, the thing that troubles me is sustaining the NEI's involvement on the one hand and secondly shifting the collaboration towards preclinical research, basic research including clinical trials and away from epidemiology and understanding the magnitude of the problem in terms of where it should be headed. But to do that again means that we've somehow got to engage our Extramural community.

Dr. Kupfer: But there's so little epidemiology going on in the Extramural community, I don't think…

Dr. Ellwein: Yeah, but there's a lot of basic science going on…

Dr. Kupfer: Yes!

Dr. Ellwein: There's a lot of preclinical…

Dr. Kupfer: That's right, oh yes

Dr. Ellwein: Yeah, so it's a natural.

Dr. Kupfer: That's what I was saying, how to squeeze out of the epidemiology.

Dr. Ellwein: Yeah, yeah.

Dr. Kupfer: Uh, the Iowa group for instance, are very active in India, but mainly to get specimens sent to them.

Dr. Ellwein: Yeah, right, right. A lot more can be done in a truly collaborative fashion.

Dr. Kupfer: That's true.

Dr. Ellwein: You missed this ARVO/NEI conference that we just had earlier this month in India, the 25 U.S. scientists who were there. Some had been India several times before and some hadn't…

Dr. Kupfer: Was Ed Stone there?

Dr. Ellwein: Ed Stone was not there.

Dr. Kupfer: Really? That's surprising.

Dr. Ellwein: The people who were there had expressed interest through ARVO. About half of those that had expressed interest were invited. Invitation means that ARVO paid for their air transport, their logging and accommodation over there. But, it was really reaching to…

Dr. Kupfer: When you say ARVO paid.

Dr. Ellwein: ARVO got a conference grant from the NEI.

Dr. Kupfer: Oh that's different.

Dr. Ellwein: Yeah, and so ARVO paid for that.

Dr. Kupfer: They were the middle man.

Dr. Ellwein: They were the middle man yeah, but having them as the middle man was very, very useful.

Dr. Kupfer: Oh, sure, oh absolutely.

Dr. Ellwein: There was a lot of value added by their participation.

Dr. Kupfer: That's right.

Dr. Ellwein: But the interactions that took place were just fantastic, and there's going to be now the second phase of this "conference" will be two days preceding the ARVO meeting this Spring in Ft. Lauderdale. And I'm sure that out of this will come a half a dozen of RO1s within the next year or so.

Dr. Kupfer: That's good.

Dr. Ellwein: I think that once this sort of catches on, once somebody sees that somebody else has got a collaboration and they see findings being published and presented I think there will be a certain amount of momentum that will catch on and it will make a difference. Not just with collaborations in India, but in China and so on, although India has an advantage in terms of their investigators being sort of almost pretty much well trained and ready to go.

Dr. Kupfer: You had mentioned about maintaining the interest internationally at NEI when you said Paul might be bit by the bug.

Dr. Ellwein: Well, yeah, I think Paul's infected. Part of it is he's got a lot of priorities for one thing, but at this NDO/US conference there were two of our council members were there.

Dr. Kupfer: Who was that?

Dr. Ellwein: Dr. Bok from UCLA and Janie Wigs from Mass Eye and Ear. They were extremely enthusiastic and gave a very strong report back to the Council meeting. So I think the approach has to be to get more people involved and take ownership in making sure these things move forward. Because, yeah, I think as NIH goes, maybe—you know there's certainly some international things going on in AIDS…

Dr. Kupfer: Oh goodness, yes.

Dr. Ellwein: A lot of activity there. It's sort of driven in a different way and there's a lot of potential.

Dr. Kupfer: There's a lot of excitement in the newspapers about the 750 scientists that wrote a letter to the NIH Director saying that…

Dr. Ellwein: Oh, yeah, I didn't see that, yeah.

Dr. Kupfer: That they were very upset because bioterrorism and that two or three organizations have a whole spectrum and he said, no that's not true, funding is much narrower.

Dr. Ellwein: Well, at first funding was diverted to AIDS and now it's being funded to bioterrorism (laughter), you know? And I don't know what the numbers are, you know the WHO has this global burden of disease figures, which is an important point. And they partly because of the data that's been generated from our studies that we've done in collaboration with them, and a better accounting for prevalence, but most importantly, recognizing that when we look at the prevalence of blindness we should not be using best corrected visual acuity but presenting visual acuity. The visual acuity they're living with—that is what counts. So, the WHO has now made a shift and reports data on presenting which has moved us up to number nine in terms of eye diseases and conditions are number nine on the global burden of disease scale. Number one I think is some psychiatric bipolar, depression, whatever are up there. Then the accounting moves toward paying attention to vision impairment less than blindness. That is to say starting at a visual acuity of 618 as being impaired, not just 360 as is blindness. The back of the envelope calculations brings us up to number three in terms of global burden of disease. So we are indeed addressing an area that's very important in terms of global health and we don't have mortality but this global burden of disease are not much, but the global burden of disease pays attention of course to morbidity, that is to say adjusted quality of life years. That when you're blind your quality of life diminishes and that's…

Dr. Kupfer: Shows a drag on the family.

Dr. Ellwein: That's a way, a metric that allow being alive with a lower quality, equating it with lives lost—years totally lost because of mortality. And that's the global burden of disease calculations which again points out the importance of vision impairment and blindness in the world.

Dr. Kupfer: Is there a publication on this?

Dr. Ellwein: Each year the WHO comes out with their annual publication—World Health Report. Each year they emphasize a different area but always back in the appendix, or at least for this last, 5, 6, 7, 8 years had been their global burden of disease calculations. And vision impairment is split up into cataract, glaucoma, age-related diseases, trachoma's in there, Onchocerciasis in there and so on. But when you take all of those and add it up, that's when I say that we are number nine.

Dr. Kupfer: Onchocerciasis seemed to have dropped off the radar screen, is that because it's being taken good care of now?

Dr. Ellwein: I suppose it's some of that—uh, you know, I'm not sure. I suppose that's probably a large part of it although there's still a lot going on you know.

Dr. Kupfer: And trachoma's still present really…

Dr. Ellwein: There's still you know, the International Trachoma Initiative.

Dr. Kupfer: Yeah.

Dr. Ellwein: It's tried to renew their efforts looking at it.

Dr. Kupfer: Yeah. There was some interesting study done.

Metchosin

Dr. Ellwein: In Metchosin, British Columbia?

Dr. Kupfer: No.

Dr. Ellwein: Ivermectin?

Dr. Kupfer: No…

Dr. Ellwein: Oh, you're talking about.

Dr. Kupfer: Trachoma.

Dr. Ellwein: Yeah, yeah, right.

Dr. Kupfer: Zithromicin.

Dr. Ellwein: Yeah, right.

Dr. Kupfer: Is that really removing the reservoir of trachoma in a community?

Dr. Ellwein: I don't know really. I think that since Onchocerciasis, and Xerophthalmia, you know are not really problems here in the U.S., in terms of the NEI's activities, they maybe would be a lower priority because there are plenty of other things that are sort of global issues.

Dr. Kupfer: Yeah. It's just that a lot of the NGO's …

Dr. Ellwein: Yeah right.

Dr. Kupfer: Have a lot of control over these things.

Dr. Ellwein: Well you can kind of target the area and focus on it.

Dr. Kupfer: Thank you very much, you were very helpful.

End of Transcript